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### Patent Application US/07/599,543E

1 2 SEQUENCE LISTING 3 (1) GENERAL INFORMATION: 4 5 APPLICANT: Opperman, Hermann 6 Ozkaynak, Engin 7 Rueger, David C. 8 Kuberasampath, Thangavel 9 (ii) TITLE OF INVENTION: Osteogenic Proteins 10 (iii) NUMBER OF SEQUENCES: 11 11 (iv) CORRESPONDENCE ADDRESS: 12 (A) ADDRESSEE: Testa Hurwitz & Thibeault 13 (B) STREET: 53 State Street 14 (C) CITY: Boston (D) STATE: Massachusetts 15 16 (E) COUNTRY: U.S.A. 17 (F) ZIP: 02109 COMPUTER READABLE FORM: 18 19 (A) MEDIUM TYPE: Diskette, 3.50 inch, 720 kb storage 20 (B) COMPUTER: IBM XT 21 (C) OPERATING SYSTEM: DOS 3.30 (D) SOFTWARE: ASC II 22 23 (vi) CURRENT APPLICATION DATA: (A) APPLICATION NUMBER: US 07/599,543 25 (B) FILING DATE: 18-Oct-90 26 (C) CLASSIFICATION: 27 (vii) PRIOR APPLICATION DATA: 28 (A) APPLICATION NUMBER: US 569,920 29 (B) FILING DATE: 20-Aug-90 (C) APPLICATION NUMBER: US 315,342 30 31 (D) FILING DATE: 23-Feb-89 (E) APPLICATION NUMBER: US 422,699 32 33 (F) FILING DATE: 17-Oct-89 34 35 36 37 38 39 40 41 42 43 44 45 46

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              (D) TOPOLOGY: linear
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          (iii) HYPOTHETICAL: no
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          (vi) ORIGINAL SOURCE:
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             (A) ORGANISM: mouse
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             (A) NAME: mOP2
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             (B) TYPE: amino acid
             (D) TOPOLOGY: linear
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          (ii) MOLECULE TYPE: protein
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          (ix) FEATURE:
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             (A) NAME: hOP2 (mature)
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#### 12/17/91 13:44:21

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# Raw Sequence Listing Patent Application US/07/599,543E

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          (iii) HYPOTHETICAL: no
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(iv) ANTI-SENSE:

#### 12/17/91 13:44:35

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            (A) NAME: hOP2
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670							Ala				TGC	1112
671	Leu	vai	19!	_	vaı	200	MIA	Ald	ser	Asp	Сув	
672	TCC	ጥጥር			CCT		AAC	CAC	СТС	CCA	CTC	1145
673											Leu	1143
674	пр	209		гуз	_	210	БÃР	изр	Leu	Gry	Leu	
675	CGC			стс			CAC	GAC	GGG	CAC	AGC	1178
676	Ara	T.eu	Tyr	Val	Glu	Thr	Glu	Agn	Glv	Hig	Ser	1170
677	9	215	-1-		220		Olu		011		DCI	
678	GTG		ССТ			GCC	GGC	CTG	СТС	GGT	CAA	1211
679							Gly					
680	225	F		-	30		23!			1	<b></b>	
681		GCC	CCA	_		CAA		_	TTC	GTG	GTC	1244
682							Gln					
683	5			40			245					
684	ACT	TTC			GCC	AGT		AGT	CCC	ATC	CGC	1277
685							Pro					
686			250	_		255					3	
687	ACC	CCT			GTG	AGG	CCA	CTG	AGG	AGG	AGG	1310
688							Pro					_
689		260	_			265			_	•	-	

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722
    CAG CCG AAG AAA AGC AAC GAG CTG CCG CAG GCC 1343
723
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724
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725
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726
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728 GGC TCC CAC GGC CGG CAG GTC TGC CGT CGG CAC
729
    Gly Ser His Gly Arg Gln Val Cys Arg Arg His
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731
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    Glu Leu Tyr Val Ser Phe Gln Asp Leu Gly Trp
732
733
              305
                         310
734 CTG GAC TGG GTC ATC GCT CCC CAA GGC TAC TCG
735
    Leu Asp Trp Val Ile Ala Pro Gln Gly Tyr Ser
736
                        320
737
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738
    Ala Tyr Tyr Cys Glu Gly Glu Cys Ser Phe Pro
739
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                    330
740 CTG GAC TCC TGC ATG AAT GCC ACC AAC CAC GCC
    Leu Asp Ser Cys Met Asn Ala Thr Asn His Ala
742 335
                   340
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743	ATC CTG CAG TCC CTG GTG CAC CTG ATG AAG CCA	1574
744	Ile Leu Gln Ser Leu Val His Leu Met Lys Pro	
745	350 355	•
746	AAC GCA GTC CCC AAG GCG TGC TGT GCA CCC ACC	1607
747	Asn Ala Val Pro Lys Ala Cys Cys Ala Pro Thr	
748	360 365	
749	AAG CTG AGC GCC ACC TCT GTG CTC TAC TAT GAC	1640
		1040
750	Lys Leu Ser Ala Thr Ser Val Leu Tyr Tyr Asp	
751	370 375	
752	AGC AGC AAC AAC GTC ATC CTG CGC AAA GCC CGC	1673
753	Ser Ser Asn Asn Val Ile Leu Arg Lys Ala Arg	
754	380 385	
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786	33.0 3.00 0.00 0.00 33.0 0.00 0.00 0.00	1 7 2 2
787	AAC ATG GTG GTC AAG GCC TGC GGC TGC CAC	1703
788	Asn Met Val Val Lys Ala Cys Gly Cys His	
789	390 395	
790	TGAGTCAGCC CGCCCAGCCC TACTGCAGCA ATTCACTGGC	1743
791	CGTCGTTTTA CAACGTGTGA CTGGGAAAAC CCTGGCGTTA	1783
792	CCCAACTTAA TCGCCTTGCA GCACATCCCC CTTTCGCCAG	1823
793	CTGGCTAATA GCGAAGAGGC CCCGCACCGA TCGCCCTTCC	1863
794		1903
795		1941
, ,,	IIIIIII NIIOOOIIN IMIIIIII	

## Raw Sequence Listing Patent Application US/07/599,543E

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796
797
798
     (2)
         INFORMATION FOR SEQ ID NO:5:
799
               SEQUENCE CHARACTERISTICS:
800
             (A) LENGTH: 98 amino acids
801
             (B) TYPE: amino acid
802
             (D) TOPOLOGY: linear
          (ii) MOLECULE TYPE: protein
803
804
          (ix) FEATURE:
805
                (D) OTHER INFORMATION: wherein "res."
806
    means "residue" and Xaa at res. 2 = (Lys or Arg); Xaa at
    res.3 = (Lys or Arg); Xaa res.9 = (Ser or Arg); Xaa at
807
808
    res.11 = (Arg or Gln); Xaa at res.16 = (Gln or Leu); Xaa
    at res. 19 = (Ile or Val); Xaa at res.23 = (Glu or Gln);
809
810
    Xaa at res.26 = (Ala or Ser); Xaa at res. 34 = (Ala or
811
    or Ser); Xaa at res.38= (Asn or Asp); Xaa at res. 40 =
812
     (Tyr or Cys); Xaa at res.49 = (Val or Leu); Xaa at
813
    res.52= (His or Asn); Xaa at res. 53 = (Phe or
814 Leu); Xaa at res. 54 = (Ile or Met); Xaa at res. 55 = (Asn
    or Lys); Xaa at res. 56 = (Glu, Asp or Asn); Xaa at res.
816
    57=(Thr, Ala or Val); Xaa at res. 61 = (Pro or Ala);
817
    Xaa at res. 67=(gln or Lys); Xaa at res. 69 =
818
    (Asn or Ser); Xaa at 71=(Ile or Thr); Xaa at res.
819
    76= (Phe or Tyr); Xaa at res. 78 = (Asp, Glu or Ser);
    Xaa at res. 80= (Ser or Asn); Xaa at res. 84 = (Ile or
    Asp); Xaa at res. 85 Arg); Xaa at res. 87 = (Tyr, Ala
    or His); and Xaa at res. 93=(Arg or Lys)
822
823
824
          (xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:
825
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827
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829
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                                   20
830
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831
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832
          Glu Gly Cys Xaa Phe Pro Leu Xaa Ser Xaa
833
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                                   40
834
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                                               Thr
835
                     45
                                  50
836
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                                               Xaa
                                                     Val
                         Xaa
                                Xaa
                                         Xaa
837
                        55
838
          Pro Lys
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### Patent Application US/07/599,543E

Xaa Ala Xaa Ser Val Leu Tyr Xaa Asp Xaa Ser Xaa Asn Val Xaa Leu Xaa Lys Xaa Pro Asn Met Val Val Xaa Ala Cys Gly Cys His INFORMATION FOR SEQ ID NO:6: (2) SEQUENCE CHARACTERISTICS: (A) LENGTH: 437 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear (ii) MOLECULE TYPE: cDNA (iii) HYPOTHETICAL: no (iv) ANTI-SENSE: (vi) ORIGINAL SOURCE: 

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919
             (A) ORGANISM: Human
920
             (F) TISSUE TYPE: placenta
921
          (ix) FEATURE:
922
            (A) NAME: OP1
923
          (xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:
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926
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927
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929
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930
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                                                    108
935 Val Ala Glu Asn Ser Ser Ser Asp Gln Arg Gln
936
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937 GCC TGT AAG AAG CAC GAG CTG TAT GTC AGC TTC
                                                    141
938 Ala Cys Lys Lys His Glu Leu Tyr Val Ser Phe
939
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                         45
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                                                    174
941 Arg Asp Leu Gly Trp Gln Asp Trp Ile Ile Ala
942
                         55
943 CCT GAA GGC TAC GCC GCC TAC TAC TGT GAG GGG
                                                    207
944 Pro Glu Gly Tyr Ala Ala Tyr Tyr Cys Glu Gly
945
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                     65
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946
     Glu Cys Ala Phe Pro Leu Asn Ser Tyr Met Asn
947
948
                    75
                               80
949
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                                                    273
     Ala Thr Asn His Ala Ile Val Gln Thr Leu Val
950
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983												
984						GAA						306
985	His	Phe			Pro	Glu	Thr	Val	Pro	Lys	Pro	
986	maa	mam	9!			100						220
987						CAG						339
988 989	Cys	-		Pro		Gln	Leu	Asn	Ala	TTE	ser	
990	CTC	109		መመረ		110 GAC	NCC.	mcc.	אאמ	CTC	אשמ	372
991						Asp						3/2
992	Vai	115	TYL		120	nap	Ser	ser	NSII	vai	TIE	
993	СТС		מממ			AAC	አጥር	CTC	CTC	ccc	GCC	405
994						Asn						40.
995	125	Lys	Lys		30	non	139	_	A 44 T	nrg	nia	
996		GGC	TGC			CTCC!			ል ጥጥር ፣	AG		437
997			Cys		1110	0100		J11Q11		.10		437
998	0,0	U-1	0,10									
999												
1000	(2)	INI	FORM	ATIO	V FO	R SE	O ID	NO:	7:			
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1003						amin						
1004						Y: :						
1005		(i:				TYP			ein			
1006				FEAT			•	-				
1007		•				NFOR	MATIO	: NC				

1008	hawain asah Ya		4an+1	
1008	wherein each Xa			, a-amino acids.
	the 20 naturally	y occurri	ig L-Isomer	, a-amino acids.
1010	(mi) CROW	NOT DECO	OTDMION. OF	0 TD NO.7.
1011	(xi) SEQU	ENCE DESC	RIPTION: SE	Q 10 NO: /:
1012				
1013	=			a Xaa Xaa Xaa
1014	1	5	10	
1015		a Xaa Xaa		a Xaa Xaa Xaa
1016	15		20	
1017			Xaa Xaa Cy	s Xaa Xaa Xaa
1018	25	30		
1019	_	a Xaa Xaa	Xaa Cys Xa	a Xaa Xaa Xaa
1020	35	40		
1021	Xaa Xaa Xa	a Xaa Xaa	Xaa Xaa Xa	a Xaa Xaa Xaa
1022	45	50	55	
1023				
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1054	Xaa Xaa Xa	a Xaa Xaa	Xaa Xaa Xa	a Xaa Xaa Cys
1055		60	65	<u> , -</u>
1056	Cys Xaa Xa	-		a Xaa Xaa Xaa
1057	70		75	
1058	· -	a Xaa Xaa		a Xaa Xaa Xaa
1059	80	85	· ·	

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Cys

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1062	Xaa Cys Xaa	
1063	100	
1064		
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1067	(A) LENGTH: 97 amino acids	
1068	(B) TYPE: amino acid	
1069	(D) TOPOLOGY: linear	
1070	(ii) MOLECULE TYPE: protein	
1071	(ix) FEATURE:	•
1072	(D) OTHER INFORMATION:	
1073	wherein each Xaa independently repre	esents one of
1074	the 20 naturally occurring L-isomer	
1075		, – ––
1076	(xi) SEQUENCE DESCRIPTION: SE	O ID NO:8:
1077	(,	<b>.</b>
1078	Xaa Xaa Xaa Xaa Xaa Xaa Xaa	a Xaa Xaa Xaa
1079	1 5 10	
1080	Xaa Xaa Xaa Xaa Xaa Xaa Xaa	a Xaa Xaa Xaa
1081	15 20	
1082	Xaa Xaa Cys Xaa Xaa Xaa Cys Xaa	a Xaa Xaa Xaa
1083	25 30	
1084	Xaa Cys Xaa Xaa Xaa Xaa Xaa Xa	a Xaa Xaa Xaa
1085	35 40	
1086	Xaa Xaa Xaa Xaa Xaa Xaa Xaa	a Xaa Xaa Xaa
1087	45 50 55	
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## Raw Sequence Listing

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                          Cys
                               Ala
                                   Pro
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                                         Tyr
                                              Tyr
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           Glu
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                                    Ile
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                 (B) TYPE: amino acid
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            (ii) MOLECULE TYPE: protein
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1249
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1263
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                                          Asn
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                                 75
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                          Ile Leu
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1266
1267
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                                          Ala
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1268
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1269
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                          Cys Ala Pro
                                               Lys
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                Ala
                     Cys
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                          Ser Val Leu
                                               Tyr
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                              Val Val Lys Ala
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1314
1315
                (D) TOPOLOGY: linear
           (ii) MOLECULE TYPE: protein
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                 (A) NAME: hOP-2S
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               Val Val
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1325 Ser Pro Ser Pro Ile Arg Thr Pro Arg
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1326		1	.5				20		
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1328 1329	Pro	Lys	25 Lys	Ser	Asn	30 Glu	Leu	Pro	Gln
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1331	Ala	Asn	Arg	Leu	Pro	Gly	Ile	Phe	Asp
1332	40			45					
1333	Asp	Val	Asn	Gly	Ser	His	Gly	Arg	Gln
1334 1335	Val	50 C	7	A	55 His		T	M	171
1336	Val	Cys	Arg O	Arg	uis	Glu	Leu 65	Tyr	Val
1337	Ser	Phe	Gln	Asp	Leu	Gly	Trp	Leu	Asp
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1339	Tyr	Val	Ile	Ala	Pro	Gln	Gly	Tyr	Ser
1340				80			_	_	
1341	Ala	Tyr	Tyr	Cys	Glu	Gly	Glu	Cys	Ser
1342	85			90					
1343	Phe	Pro	Leu	Asp	Ser	Сув	Met	Asn	Ala
1344	mb	95	TT 2	21.	100		G1	0	<b>7</b>
1345 1346	Thr	Asn 10	His	Ala	Ile	Leu	Gln	Ser	Leu
1347	Val	His	Leu	Met	Lys	Pro	.10 Asn	71-	Val
1347	Val	ura	11		Lys	PLO	120	Ala	Val
1349	Pro	Lys	Ala		Cys	Ala		Thr	Lys
1350		-1-		125	0,10				_,_
1351									
1352									
1353									
1354									
1355									
1356									
1357									
1358									
1359									
1360									
1361 1362									
1362									
1364									
1365									
1000									

12/17/91 13:46:33

1379									
1380									
1381									
1382	Leu	Ser	Ala	Thr	Ser	Val	Leu	Tyr	Tyr
1383	130			135					
1384	Asp	Glu	Ser	Asn	Asn	Val	Ile	Leu	Arg
1385		140			145				
1386	Lys	Ala	Arg	Asn	Met	Val	Val	Lys	Ala
1387		15	0			1	.55		
1388	Cys	Gly	Cys	His					
1389			16	0					

PAGE: 1

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EQUENCE VERIFICATION REPORTS
ATENT APPLICATION US/07/5 543E

DATE: 12/17/91 TIME: 13:46:34

#### L-INE ERROR

ORIGINAL TEXT

24 Wrong application Serial Number 809 Response Exceeds Line Limitations 810 Response Exceeds Line Limitations 811 Response Exceeds Line Limitations 812 Response Exceeds Line Limitations 813 Response Exceeds Line Limitations 814 Response Exceeds Line Limitations 815 Response Exceeds Line Limitations 816 Response Exceeds Line Limitations 817 Response Exceeds Line Limitations 818 Response Exceeds Line Limitations 819 Response Exceeds Line Limitations 820 Response Exceeds Line Limitations 821 Response Exceeds Line Limitations 822 Response Exceeds Line Limitations

(A) APPLICATION NUMBER: US 07/599,543 at res. 19 = (Ile or Val); Xaa at res.23 Xaa at res.26 = (Ala or Ser); Xaa at res or Ser); Xaa at res.38= (Asn or Asp); Xa (Tyr or Cys); Xaa at res.49 = (Val or Le res.52= (His or Asn); Xaa at res.53 = (Leu); Xaa at res.54 = (Ile or Met); Xaa or Lys); Xaa at res.56 = (Glu, Asp or A 57=(Thr, Ala or Val); Xaa at res.61 = (Xaa at res.67=(gln or Lys); Xaa at res.(Asn or Ser); Xaa at 71=(Ile or Thr); Xa 76= (Phe or Tyr); Xaa at res.78 = (Asp, Xaa at res.80= (Ser or Asn); Xaa at res.8 or His); and Xaa at res.93=(Arg or Lys)

PAGE: 1

SEQUENCE MISSING ITEM REPORT. ATENT APPLICATION US/07/50 543E

DATE: 12/17/91 TIME: 13:46:34

MANDATORY IDENTIFIER THAT WAS NOT FOUND

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PAGE: 1

REQUENCE CORRECTION REPORT DATE: 12/17/91 TIME: 13:46:34

### LINE ORIGINAL TEXT

76 (A) NAME: MOF2 (MINISTREE NOP2 (MINISTREE N 922 (A) NAME: OP1 1137 (A) NAME: hOP-2P 1213 (A) NAME: hOP-2R

1318 (A) NAME: hOP-2S

#### CORRECTED TEXT

(A) NAME/KEY: mOP2 (mature)

(A) NAME/KEY: mOP2

(A) NAME/KEY: hOP2 (mature)

(A) NAME/KEY: hOP2 (A) NAME/KEY: OP1 (A) NAME/KEY: hOP-2P (A) NAME/KEY: hOP-2R

(A) NAME/KEY: hOP-2S